CLAIMS

What is claimed is:

1. A method of screening for inhibitors of beta-amyloid production comprising,

1) contacting a potential inhibitor of beta-amyloid production and a tagged inhibitor of beta-amyloid production with at least one macromolecule involved in the processing of APP and the production of beta-amyloid peptide, said macromolecule containing a binding site specific for said tagged inhibitor of beta-amyloid production;

2) separating the tagged inhibitor of beta-amyloid production bound to said macromolecule from the tagged inhibitor of beta-amyloid production free from said macromolecule; and

3) determining an inhibitory concentration of the potential inhibitor of beta-amyloid production from the concentration of tagged inhibitor of beta-amyloid production bound to said macromolecule.

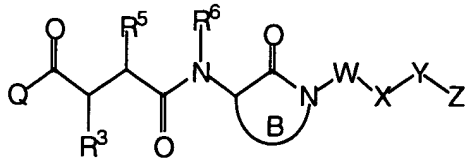
2. The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production, a fluoroscence labeled inhibitor of beta-amyloid production or a biotin labeled inhibitor of beta-amyloid production.

3. The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production.

4. The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a tritium or iodine radiolabeled inhibitor of beta-amyloid production.

5. The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a tritium radiolabeled inhibitor of beta-amyloid production.

6. The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I):



(I)

wherein:

at least one atom of the compound of the Formula (I) is radiolabeled;

Q is NH_2;

R^3 is C_1-C_6 alkyl substituted with 0-1 R^4;

R^4 is H, OH, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} carbocycle, C_6-C_{10} aryl, or 5 to 10 membered heterocycle;

R^5 is H, OR^{14};
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_1-C_6 alkoxy substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};

C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

W is $-(CR^8R^{8a})_p-$;

p is 0 to 4;

R^8 and R^{8a}, at each occurrence, are independently selected from H, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-3 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

Y is a bond or $-(CR^9R^{9a})_t-V-(CR^9R^{9a})_u-$;

t is 0 to 3;

u is 0 to 3;

R^9 and R^{9a}, at each occurrence, are independently selected from H, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, -$S(=O)_2$-, -$N(R^{19})$-, -$C(=O)NR^{19b}$-, -$NR^{19b}C(=O)$-, -$NR^{19b}S(=O)_2$-, -$S(=O)_2NR^{19b}$-, -$NR^{19b}S(=O)$-, -$S(=O)NR^{19b}$-, -C(=O)O-, or -OC(=O)-;

Z is H;
C_1-C_8 alkyl substituted with 0-2 R^{12};
C_2-C_4 alkenyl substituted with 0-2 R^{12};
C_2-C_4 alkynyl substituted with 0-2 R^{12};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12} is C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

B is a 5 to 10 membered lactam, wherein the lactam is saturated, partially saturated or unsaturated; wherein each additional lactam carbon is substituted with 0-2 R^{11}; and, optionally, the lactam contains a heteroatom selected from -O-, -S-, -S(=O)-, -$S(=O)_2$-, -N=, and -$N(R^{10})$-;

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl optionally substituted with R^{10a};

C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{11} is C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same carbon atoms may be combined to form a C_3-C_6 carbocycle;

alternatively, two R^{11} substituents on adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical, wherein said benzo fused radical is substituted with 0-3 R^{13};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{11b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl);

R^{17} is H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl);

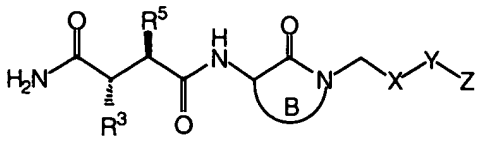
R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl; and

R^{20} is H or C_1-C_6 alkyl.

7. The method of Claim 6 wherein R^3 is C_3-C_6 alkyl.

8. The method of Claim 6 wherein R^3 is C_3-C_6 alkyl substituted with about 1 to about 4 ^3H.

9. The method of Claim 6 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (II):



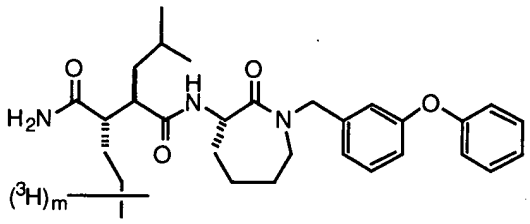
(II)

wherein:

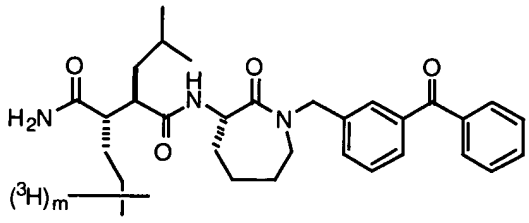
at least one atom of the compound of the Formula (II) is radiolabeled.

10. The method of Claim 9 wherein R^3 is C_3-C_6 alkyl substituted with about 1 to about 4 ^3H.

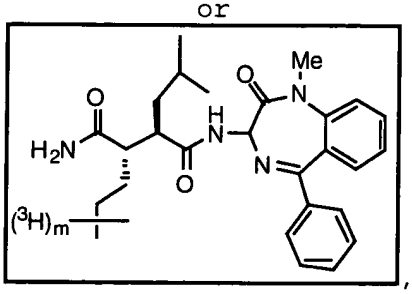
11. The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a compound of Formula:



or

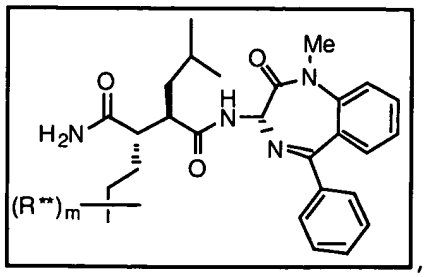


or



wherein m is about 2.

12. The method of Claim 1 wherein the tagged inhibitor of beta-amyloid production comprises a compound of Formula (I-43T):



(I-43T)

wherein m is about 2.

13. The method of Claim 1 wherein at least one macromolecule involved in the processing of APP and the production of beta-amyloid peptide comprises presenilin 1 or a fragment of presenilin 1.

14. The method of Claim 1 wherein at least one macromolecule involved in the processing of APP and/or the production of beta-amyloid peptide comprises comprises:

(1) presenilin-1;
(2) presenilin-2;
(3) β secretase;
(4) α secretase;
(5) γ secretase; or
(6) BACE/memapsin 2;

or any fragment or derivative thereof.

15. The method of Claim 1 wherein the inhibitory concentration is half maximal inhibitory concentration.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of an inhibitor of beta-amyloid production identified by the screening assay of Claim 1 or a pharmaceutically acceptable salt or prodrug form thereof.

17. A method for treating degenerative neurological disorders involving beta-amyloid production comprising administering to a host in need of such treatment a therapeutically effective amount of an inhibitor of beta-amyloid production identified by the screening assay of Claim 1 or a pharmaceutically acceptable salt or prodrug form thereof.

18. A method for treating Alzheimer's disease comprising administering to a host in need of such treatment a therapeutically effective amount of an inhibitor of beta-amyloid production identified by the screening assay of Claim 1 or a pharmaceutically acceptable salt or prodrug form thereof.

19. A method of identifying a macromolecule involved in APP processing comprising

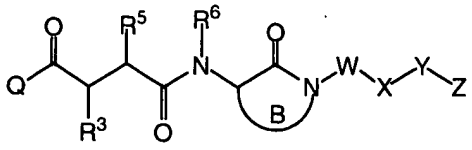
1) contacting a tagged inhibitor of beta-amyloid production with material suspected to contain a macromolecule involved in APP processing;
2) separating a complex comprising a tagged inhibitor of beta-amyloid production and a macromolecule involved in APP processing; and
3) identifying the complex.

20. The method of Claim 19 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production, a fluoroscence labeled inhibitor of beta-amyloid production, a biotin labeled inhibitor of beta-amyloid production, a photoaffinity labeled inhibitor of beta-amyloid production, or any combination of tags thereof in one inhibitor of beta-amyloid production.

21. The method of Claim 19 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production.

22. The method of Claim 19 wherein the tagged inhibitor of beta-amyloid production comprises a tritium labeled inhibitor of beta-amyloid production.

23. The method of Claim 19 wherein the tagged inhibitor of beta-amyloid production comprises a compound of Formula (I):



(I)

wherein:

at least one atom of the compound of the Formula (I) is radiolabeled;

Q is NH_2;

R^3 is C_1-C_6 alkyl substituted with 0-1 R^4;

R^4 is H, OH, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} carbocycle, C_6-C_{10} aryl, or 5 to 10 membered heterocycle;

R^5 is H, OR^{14};
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_1-C_6 alkoxy substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;

C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

W is $-(CR^8R^{8a})_p-$;

p is 0 to 4;

R^8 and R^{8a}, at each occurrence, are independently selected from H, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-3 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

Y is a bond or $-(CR^9R^{9a})_t-V-(CR^9R^{9a})_u-$;

t is 0 to 3;

u is 0 to 3;

R^9 and R^{9a}, at each occurrence, are independently selected from H, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;
C_1-C_8 alkyl substituted with 0-2 R^{12};
C_2-C_4 alkenyl substituted with 0-2 R^{12};
C_2-C_4 alkynyl substituted with 0-2 R^{12};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12} is C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

B is a 5 to 10 membered lactam, wherein the lactam is saturated, partially saturated or unsaturated; wherein each additional lactam carbon is substituted with 0-2 R^{11}; and, optionally, the lactam contains a heteroatom selected from -O-, -S-, $-S(=O)-$, $-S(=O)_2-$, -N= and $-N(R^{10})-$;

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;

C_1-C_6 alkyl optionally substituted with R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle optionally substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{10b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{11} is C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle substituted with 0-3 R^{11b};

alternatively, two R^{11} substituents on the same carbon atoms may be combined to form a C_3-C_6 carbocycle;

alternatively, two R^{11} substituents on adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle or a benzo fused radical, wherein said benzo fused radical is substituted with 0-3 R^{13};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, phenyl or CF_3;

R^{11b}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, or CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl);

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl);

R^{17} is H, phenyl, benzyl, C_1-C_6 alkyl, or C_2-C_6 alkoxyalkyl;

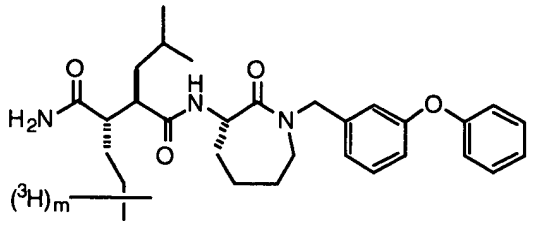
R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl); and

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, -C(=O)-(C_1-C_6 alkyl) and -S(=O)$_2$-(C_1-C_6 alkyl);

R^{19b} is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, phenyl, benzyl or phenethyl; and

R^{20} is H or C_1-C_6 alkyl.

24. The method of Claim 19 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I-7T):



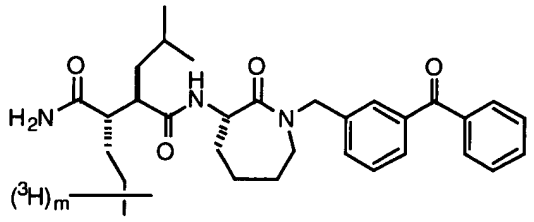
(I-7T)

wherein m is about 2.

25. The method of Claim 19 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I-43T), wherein m is about 2.

26. The method of Claim 20 wherein the tagged inhibitor of beta-amyloid production is radiolabeled and photoaffinity labeled.

27. The method of Claim 20 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I-11T):



(I-11T)

wherein m is about 2.

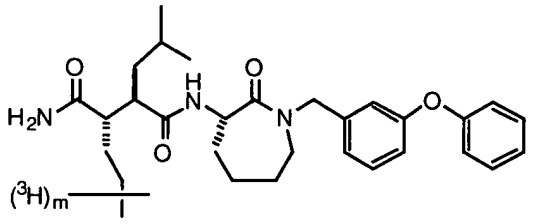
28. A macromolecule involved in APP processing comprising a macromolecule to which a tagged inhibitor of beta-amyloid production binds to specifically.

29. A macromolecule of Claim 28 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production, a

fluoroscence labeled inhibitor of beta-amyloid production, a biotin labeled inhibitor of beta-amyloid production, a photoaffinity labeled inhibitor of beta-amyloid production, or any combination of tags thereof in one inhibitor of beta-amyloid production.

30. A macromolecule of Claim 28 wherein the tagged inhibitor of beta-amyloid production comprises a radiolabeled inhibitor of beta-amyloid production.

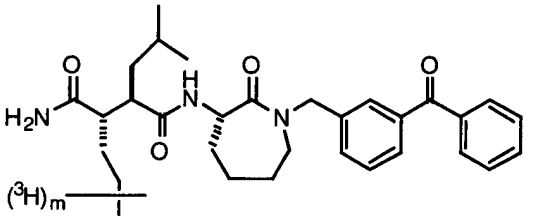
31. A macromolecule of Claim 28 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I-7T):



(I-7T)

wherein m is about 2.

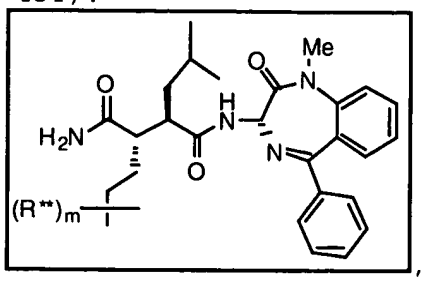
32. A macromolecule of Claim 28 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I-11T):



(I-11T)

wherein m is about 2.

33. A macromolecule of Claim 28 wherein the tagged inhibitor of beta-amyloid production comprises a compound of the Formula (I-43T):



(I-43T)

wherein m is about 2.

34. The macromolecule of Claim 28 comprising presenilin 1 or a fragment of presenilin 1.

35. The macromolecule of Claim 28 comprising presenilin 2 or a fragment of presenilin 2.

36. An inhibitor of beta-amyloid production comprising a compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I-7T) or (I-43T) wherein m is about 2.

37. An inhibitor of beta-amyloid production of Claim 36 wherein the macromolecule involved in the production of beta-amyloid peptide is presenilin 1 or a fragment of presenilin 1.

38. An inhibitor of beta-amyloid production of Claim 36 wherein the macromolecule involved in the production of beta-amyloid peptide is presenilin 2 or a fragment of presenilin 2.

39. An inhibitor of beta-amyloid production of Claim 36 comprising a compound which interacts with a binding site on a macromolecule involved in the production of beta-

amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I-7T) wherein m is about 2; and the compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

40. An inhibitor of beta-amyloid production of Claim 36 comprising a compound which interacts with a binding site on presenilin 1 or a fragment of presenilin 1; wherein said binding site is a specific binding site for a compound of Formula (I-7T) wherein m is about 2; and the compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

41. An inhibitor of beta-amyloid production of Claim 36 comprising a compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I-43T) wherein m is about 2; and the compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

42. An inhibitor of beta-amyloid production of Claim 36 comprising a compound which interacts with a binding site on presenilin 1 or a fragment of presenilin 1; wherein said binding site is a specific binding site for a compound of Formula (I-43T) wherein m is about 2; and the compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

43. A tagged inhibitor of beta-amyloid production comprising a tagged compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I-7T) or (I-43T) wherein m is about 2.

44. A tagged inhibitor of beta-amyloid production of Claim 43 wherein the macromolecule involved in the production of beta-amyloid peptide is presenilin 1 or a fragment of presenilin 1.

45. A tagged inhibitor of beta-amyloid production of Claim 43 wherein the macromolecule involved in the production of beta-amyloid peptide is presenilin 2 or a fragment of presenilin 2.

46. A tagged inhibitor of beta-amyloid production of Claim 43 comprising a tagged compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I-7T) wherein m is about 2; and the tagged compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

47. A tagged inhibitor of beta-amyloid production of Claim 43 comprising a tagged compound which interacts with a binding site on presenilin 1 or a fragment of presenilin 1; wherein said binding site is a specific binding site for a compound of Formula (I-7T) wherein m is about 2; and the tagged compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

48. A tagged inhibitor of beta-amyloid production of Claim 43 comprising a tagged compound which interacts with a binding site on a macromolecule involved in the production of beta-amyloid peptide; wherein said binding site is a specific binding site for a compound of Formula (I-43T) wherein m is about 2; and the tagged compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

49. A tagged inhibitor of beta-amyloid production of Claim 43 comprising a tagged compound which interacts with a binding site on presenilin 1 or a fragment of presenilin 1; wherein said binding site is a specific binding site for a compound of Formula (I-43T) wherein m is about 2; and the tagged compound demonstrates a half maximal inhibitory concentration less than 10 micromolar for beta-amyloid production.

50. A method of identifying inhibitors as therapeutics for neurological and other disorders involved in APP processing and beta-amyloid production comprising

(1) contacting at least one macromolecule involved in APP processing and beta-amyloid production, which macromolecule a tagged inhibitor of beta-amyloid production binds to specifically, with a potential beta-amyloid inhibitor; and

(2) determining the level of inhibition of APP processing and beta-amyloid production.

51. The method of Claim 50 wherein the macromolecule is a complex of macromolecules.

52. The method of Claim 50 wherein the macromolecule is presenilin 1 or a fragment of presenilin 1.

53. The method of Claim 50 wherein the macromolecule is presenilin 2 or a fragment of presenilin 2.

54. A method of treating Alzheimer's disease comprising administering to a host in need of such treatment a therapeutically effective amount of an inhibitor of beta-amyloid production, or a pharmaceutically acceptable salt or prodrug form thereof, wherein said inhibitor of beta-amyloid production binds to a binding site on a macromolecule involved in the production of beta-amyloid peptide and effects a decrease in production of beta-amyloid peptide;

wherein said binding site is a specific binding site for a compound of Formula (I-7T) or (I-43T) wherein m is about 2.

55. The method of Claim 54 wherein the macromolecule comprises presenilin-1, a fragment of presenilin-1, presenilin-2, or a fragment of presenilin-2.

56. A method of Claim 54 wherein the binding site is a specific binding site for a compound of Formula (I-43T) wherein m is about 2.

57. The method of Claim 56 wherein the macromolecule comprises presenilin-1 or a fragment of presenilin-1.

58. The method of Claim 56 wherein the macromolecule comprises presenilin-2 or a fragment of presenilin-2.

59. A method of in vivo diagnostic imaging comprising administering to a subject a diagnostically effective amount of a radiolabeled inhibitor of beta-amyloid production.

60. A method of Claim 59 wherein said method is used in the diagnosis of a neurological disease which involves APP processing or elevated levels of beta-amyloid, or both.

61. A method of Claim 59 wherein said method is used in the diagnosis of Alzheimer's disease.

62. A method of Claim 59 wherein the radiolabeled inhibitor is suitable for imaging of the brain of the subject.

63. A method of Claim 59 wherein the radiolabeled inhibitor is radiolabeled with one or more radioisotope selected from ^{3}H, ^{11}C, ^{14}C, ^{18}F, ^{32}P, ^{35}S, ^{123}I, ^{125}I, or ^{131}I.

64. A method of Claim 59 wherein the inhibitor of beta-amyloid production is a compound selected from any compound disclosed in or within the scope of compounds disclosed in a reference selected from:

(1) United States patent US 5,703,129;
(2) PCT application WO98/22441 (or its priority USSN 08/755,444);
(3) PCT application WO98/22433 (or its priority USSN 08/807,538);
(4) PCT application WO98/22430 (or its priority USSN 08/754,895);
(5) PCT application WO98/22493 (or its priority USSN 08/755,334);
(6) PCT application WO98/22494 (or its priorities USSN 08/808,528, 08/807,528 or 08/807,427);
(7) PCT application WO98/28268 (or its priority USSN 08/780,025);
(8) PCT application WO98/38177;
(9) PCT application WO95/09838
(10) PCT application WO99/67221;
(11) PCT application WO99/67220;
(12) PCT application WO99/67219;
(13) PCT application WO95/66934;
(14) PCT application WO00/24392; or
(15) Ghosh et al., JACS (2000) 122:3522-2523;

or any compound which inhibits beta-amyloid production and binds competitively with any of the foregoing compounds in any of the assays described in the Utility section hereof;

all of which foregoing references are hereby incorporated by reference in their entirety.

65. A method of Claim 59 wherein the inhibitor of beta-amyloid production exhibits activity as an inhibitor in the method of any of Claim 1.

66. A method of Claim 59 wherein the inhibitor of beta-amyloid production binds to a macromolecule which is capable of being identified by the method of any of Claim 19.

67. A method of Claim 59 wherein the inhibitor of beta-amyloid production binds to a macromolecule of any of Claim 28.

68. A method of Claim 59 wherein the inhibitor of beta-amyloid production is selected from an inhibitor of any of Claim 36.

69. A method of Claim 59 wherein the radiolabeled inhibitor of beta-amyloid production is a radiolabeled tagged inhibitor of any of Claims 43.

70. A method of Claim 59 wherein the inhibitor of beta-amyloid production is selected from:

(1) an inhibitor of presenilin-1;
(2) an inhibitor of presenilin-2;
(3) an inhibitor of β secretase;
(4) an inhibitor of α secretase;
(5) an inhibitor of γ secretase; or
(6) an inhibitor of BACE/memapsin 2.

71. A pharmaceutical composition suitable for in vivo diagnostic imaging comprising a radiolabeled inhibitor of beta-amyloid production.

72. A pharmaceutical composition of Claim 71 wherein the composition is used in the diagnosis of a neurological disease which involves APP processing or elevated levels of beta-amyloid, or both.

73. A pharmaceutical composition of Claim 71 wherein the composition is used in the diagnosis of Alzheimer's disease.

74. A pharmaceutical composition of Claim 71 wherein the radiolabeled inhibitor is suitable for imaging of the brain of the subject.

75. A pharmaceutical composition of Claim 71 wherein the radiolabeled inhibitor is radiolabeled with one or more radioisotope selected from ^{3}H, ^{11}C, ^{14}C, ^{18}F, ^{32}P, ^{35}S, ^{123}I, ^{125}I, or ^{131}I.

76. A pharmaceutical composition of Claim 71 wherein the inhibitor of beta-amyloid production is a compound selected from any compound disclosed in or within the scope of compounds disclosed in a reference selected from:

(1) United States patent US 5,703,129;
(2) PCT application WO98/22441 (or its priority USSN 08/755,444);
(3) PCT application WO98/22433 (or its priority USSN 08/807,538);
(4) PCT application WO98/22430 (or its priority USSN 08/754,895);
(5) PCT application WO98/22493 (or its priority USSN 08/755,334);
(6) PCT application WO98/22494 (or its priorities USSN 08/808,528, 08/807,528 or 08/807,427);
(7) PCT application WO98/28268 (or its priority USSN 08/780,025);
(8) PCT application WO98/38177;
(9) PCT application WO95/09838;
(10) PCT application WO99/67221;
(11) PCT application WO99/67220;
(12) PCT application WO99/67219;
(13) PCT application WO95/66934;
(14) PCT application WO00/24392; or

(15) Ghosh et al., JACS (2000) 122:3522-2523;

or any compound which inhibits beta-amyloid production and binds competitively with any of the foregoing compounds in any of the assays described in the Utility section hereof;

all of which foregoing references are hereby incorporated by reference in their entirety.

75. A pharmaceutical composition of Claim 71 wherein the inhibitor of beta-amyloid production is selected from:

(1) an inhibitor of presenilin-1;
(2) an inhibitor of presenilin-2;
(3) an inhibitor of β secretase;
(4) an inhibitor of α secretase;
(5) an inhibitor of γ secretase; or
(6) an inhibitor of BACE/memapsin 2.